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10/574,227	04/21/2006	Christian Heinis	27280U	2146

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EXAMINER	
DESAI, ANAND U	
ART UNIT	PAPER NUMBER
1656	
MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/574,227	HEINIS, CHRISTIAN	
	Examiner	Art Unit	
	Anand U. Desai, Ph.D.	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 June 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) *7 drawn to rRNA and mRNA species* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *31 March 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of the species identified as DNA in the reply filed on June 28, 2007 is acknowledged. The traversal is on the ground(s) that the instant subject matter is directed to a method for producing nucleotides bonded to their corresponding polypeptides by in vitro translation of the nucleic acids in compartments consisting of a water-in-oil emulsion and therefore the present subject matter does define a contribution over the prior art. Further, a complete and thorough search for the invention set forth in any one of the species would not be a serious burden.

This is not found persuasive because the species are not obvious variants of each other based on the current record. DNA, rRNA, and mRNA are different chemical structure with different functions. There is an examination and search burden for these patentably distinct species due to their mutually exclusive characteristics. The species require a different field of search (e.g., searching different classes/subclasses or electronic resources, or employing different search queries).

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable generic claim as provided by 37 CFR 1.141.

The requirement is still deemed proper and is therefore made FINAL.

2. Claim 7 drawn to rRNA, and mRNA are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species, there being no allowable generic or

linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on June 28, 2007.

3. Claims 1-19 as drawn to the species DNA are currently under examination.

Priority

4. Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d). Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file. The priority date is October 1, 2003.

Specification

5. The disclosure is objected to because of the following informalities:

6. The brief description of the drawing section is not identified by a title and the description does not describe the variables in each respective figure legend. Suggest describing figures by identifying variables in each figure.

7. The abstract is objected because of legal phraseology. The word, "Said" in the 2nd line of the abstract should be avoided. Applicant is reminded of the proper language and format for an abstract of the disclosure. The legal phraseology often used in patent claims, such as "means" and "said," should be avoided.

Appropriate correction is required.

Claim Rejections - 35 USC § 101

8. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

9. Claims 18 and 19 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 112

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 1, and 17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

12. Claim 1 recites the limitation "the fusion polypeptides" in the first line of step b). There is insufficient antecedent basis for this limitation in the claim. Suggest, “a fusion polypeptide”.

13. Claim 17 recites the limitation "the modified nucleic acid" in the first line. There is insufficient antecedent basis for this limitation in the claim.

14. Claims 18, and 19 provides for the use of cytosine-5-methyl transferase, and fusion polypeptide complexes, respectively, but, since the claim does not set forth any steps involved in

the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claim Rejections - 35 USC § 103

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

16. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

17. Claims 1-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Epstein (U.S. Patent 5,856,090) in view of Doi and Yanagawa (FEBS Lett 457(2): 227-230 (1999)).

Epstein developed plasmids and methods that provide covalent linkage between genetic information and peptides or proteins encoded by the genetic information, resulting in a plasmid-polypeptide determinant conjugate. The linkage is stable, allowing both the plasmid and the polypeptide determinant to be manipulated. A plasmid according to the present invention comprises: (1) a gene fusion construct including a gene encoding a DNA methylase and a gene

encoding a polypeptide determinant covalently joined, either directly or through a linker, the gene fusion construct encoding a gene fusion product including a cytosine (C-5) DNA methylase having a methyltransferase activity and a polypeptide determinant covalently joined thereto, either directly or through a peptide linker; (2) a promoter operatively linked to the gene fusion construct for promoting transcription of the gene fusion construct as messenger RNA; and (3) a methylase conjugation element linked to the gene fusion either directly or through an intervening sequence, the methylase conjugation element including a methylase binding site having at least one copy of a nucleotide sequence including a cytidine suicide analog capable of irreversibly binding the cytosine (C-5) DNA methylase within the gene fusion product. Typically, the cytidine suicide analogue is 2'-deoxy-5-fluorocytidine, 2'-deoxy-5-azacytidine, or 2'-pyrimidinone-1-.beta.-D-2-deoxyriboside. Preferably, the cytidine suicide analog is 2'-deoxy-5-azacytidine; an alternative is 2'-deoxy-5-fluorocytidine. Typically, the methylase conjugation element includes 1 to 50 copies of the methylase binding site having a specificity for the cytosine (C-5) DNA methylase. More typically, the methylase conjugation element includes 3 to 20 copies of the methylase binding site; preferably, it includes 4 to 6 copies of the methylase binding site. The gene fusion construct can have the DNA methylase gene covalently joined contiguously in-frame to the polypeptide determinant gene with a linking orientation selected from the group consisting of a first orientation with the 5'-terminus of the DNA methylase gene covalently joined to the 3'-terminus of the polypeptide determinant gene and a second orientation in which the 3'-terminus of the DNA methylase gene is covalently linked to the 5'-terminus of the polypeptide determinant gene. The cytosine (C-5) DNA methylase can be one of Aqu I, Eag I, Eco 72 I, Hga I-1, Hga I-2, Hha I, Hpa II, Msp I, Nae I, Sss I, EcoR II, Hae III, NgoP II, Fnu

D, Nla III, ScrF I, Sin I, Sso II, BsuF I, NgoM I, or Arabt. The nucleotide sequence of the methylase binding site of the methylase conjugation element is capable of serving as a substrate for the cytosine (C-5) DNA methylase used. Typically, the methylase is Msp I, Aqu I, or Hha I. Alternatively, the method can omit the deproteinization step, in which case the isolation of the nucleic acid segment that encodes the polypeptide determinant having at least one altered property can be performed by amplifying the nucleic acid segment encoding the polypeptide determinant with the at least one altered property by a sequence-specific primer-based amplification method employing at least two primers, such as PCR (see claims 36-46). Epstein does not disclose the use of water-in-oil emulsion microcompartments for in vitro expression.

Doi and Yanagawa disclose the binding of streptavidin-polypeptide conjugates to the biotinylated nucleic acid encoding these in microcompartments. The cis conjugation of genotype and phenotype the streptavidin-polypeptide conjugates are transcribed and translated in aqueous compartments in a water-in-oil emulsion. Each compartment contains at most one nucleic acid. After the translation of the streptavidin-polypeptide conjugates these can bind to the biotinylated DNA in the compartment. The polypeptide-nucleic acid conjugates may subsequently be extracted from the emulsion and be subjected to a selection method based on the desired properties.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to produce a nucleic acid polypeptide conjugate using the water-in-oil emulsion microcompartment, because Doi and Yanagawa disclose the in vitro transcription-translation in a

water-in-oil emulsion and subsequent nucleic acid polypeptide conjugation. Additional motivation of using microcompartments is provided by the known desire to prevent contaminants from degrading the nucleic acid and amino acid molecules.

Furthermore in reference to the rejection of claim 12, "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). Generally, differences in microcompartment size will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration is critical.

Conclusion

18. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anand U. Desai, Ph.D. whose telephone number is (571) 272-0947. The examiner can normally be reached on Monday - Friday 9:00 a.m. - 5:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Kathleen Kerr Bragdon can be reached on (517) 272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

September 15, 2007

AD
/Anand Desai/
Patent Examiner
Art Unit 1656